7-17-2017

Comparison of White Spot Lesions among Clear Aligners, Self-Ligating Brackets and Conventional Brackets - A Randomized Controlled Clinical Trial

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BChD - Leeds Dental Institute, The University of Leeds, UK, 2011

A Thesis
Submitted in Partial Fulfillment of the
Requirements for the Degree of
Master of Dental Science
at the
University of Connecticut,
2017

APPROVAL PAGE

Master of Dental Science Thesis

Comparison of White Spot Lesions among Clear Aligners, Self-Ligating Brackets and Conventional Brackets - A Randomized Controlled Clinical Trial

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2017

ACKNOWLEDGEMENT

I would like to sincerely thank my major advisor Dr. Ravindra Nanda for two matters. First for allowing me to part of this prestigious program and secondly for giving me all the support I needed during my orthodontic training. I am honoured to learn from one of the well-recognised figures in field of orthodontics who not only taught me contemporary orthodontics but also took me in a journey through the history of orthodontia.

I would also like to acknowledge Dr. Flavio Uribe for all the help and education he offered to me. His enthusiasm, passion, analytical approaches and pursuit of perfection are inspirational. Despite being the director of programme, he always has the desire to learn more and improve. Such eagerness taught me that in order to be a great orthodontist, one must seek endless education so as to expand their knowledge and skills.

I am very thankful to Dr. Madhur Upadhyay for guiding me through my research and for his great contribution to my understanding of the biomechanical foundation orthodontic therapy. Such contribution will definitely add to my confidence in clinically treating people who are in need of braces efficiently and effectively.

I would also like to express my appreciation to my other committee members Dr. Sachin Agarwal, Dr. Aadarsh Gopalakrishna along with the faculty of the Division of Orthodontics for being very supportive over these past three years. I also want to thank Chia-Ling Kuo for her help with the statistics.

I would also like to thank my friends back home for encouraging me and pushing me forward in helping me achieve my goals and dreams, without whom this task would be more daunting.

Finally, I am indeed indebted to my parents who without them I would not reach where I am today. Their endless love, support, and encouragement, have always made me stronger and eager to chase better education so as to improve myself.

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INTRODUCTION

Objective of Research

To compare the incidence and the severity of White Spot Lesions among clear aligners, self-ligating and conventional orthodontic brackets appliance systems after 9 and 18 months of orthodontic treatment in a randomized clinical trial.

Review of Literature

Recently, the orthodontic patient population has expanded dramatically to include not only children and adolescents, but also adults. Such increase comes with a parallel trend in the demand of an aesthetic alternative to conventional fixed appliances[1,2]. Apart from their unaesthetic appearance, conventional braces do have other negative issues such as compromising the ability of the patient to perform and maintain optimal oral hygiene, increased risk of periodontal breakdown as a result of plaque build-up, increased risk of root resorption, increased risk of white spot lesions, and the need of multiple follow-up visits as to reactivate and adjust the appliance[1-8]. Of course, all these drawbacks of treatment are also major dento-legal concern for the operating practitioner[6-8]. Perhaps white spot lesions "also known as early enamel caries or demineralization" are the most common iatrogenic side effect, among the aforementioned, of orthodontic treatment with highly variable occurrence reported in the literature ranging from 2-96%[9-17]. According to Øgaard (1989), patients receiving fixed orthodontic treatment are more prone to white spot lesions as compared to those receiving no fixed appliances[18].

Orthodontic appliances including bands, brackets, and arch wires act as plaque-retentive factors hence increasing the chance plaque accumulation[11,15,19-22]. Subsequently, the level of Streptococcus *mutans*, a cariogenic bacterium, rises in the oral environment[23-25]. The presence of such species results in a constant lowering of the pH level of the oral cavity hence impairing the remineralization process while enhancing the demineralization of the tooth

tissue[26,27]. If such process continues for four weeks, then white spot lesions could be detected on the clinical level[21,28]. Therefore, it seems logical that the reduction of plaque build-up would directly influence the development of white spot lesions.

Self-ligating brackets and clear aligner therapy are more recent advents in the field orthodontics when compared the conventional brackets. Manufacturers of these two different appliances claim that plaque retention is reduced in an attempt to address some of iatrogenic damage associated with conventional braces[29-31]. Nonetheless, such claims are not based on strong clinical evidence. Currently, most of these assertions are based on case reports, case series, surveys, anecdotal reports and retrospective studies[30,32]. In a pilot study, self-ligating brackets have been shown to reduce plaque retention when compared to conventional brackets 5-week post-treatment[33]. After one-year follow-up of the same patients, neither plaque level nor white spot lesions showed statistical significance in the two different bracket types[34]. However, the follow up study was weak with a sample size of 13 patients only.

Moreover, it seems intuitive to think that clear 'removable' aligners promote better oral hygiene, however; a case series study has shown that such appliance could cause severe demineralization of the enamel surfaces[35]. The use of Invisalign® as an orthodontic treatment option has been growing immensely since its launch. According to Miethke *et. al.* (2005) and Kunico *et. al.* (2007) more than 300,000 patients treated with this appliance[36,37]. Align Tech® reports that about 2.6 million patients start Invisalign treatment each year[38]. In addition, a recent survey of two thirds of the US orthodontic residency program, about 84% of the residents claimed that they will be highly likely to use the system for treating their patients[31].

Despite this increasing usage of this system, there is still a lack of substantial scientific evidence through clinical trials highlighting its biological compatibility, efficacy, and its possible side effects including root resorptions and white spot lesions[30,32].

Despite a thorough search of the literature, no study could be located in which a comparison between fixed braces and removable aligner appliances in terms of white spot lesions incidence was made. Only one study was found that compares the effect of fixed and functional (removable) appliances on enamel decalcifications in early Class II treatment[39]. In this study, one group had the Bionator as a removable appliance, a second group had molar bands which allow the delivery of the headgear as a fixed appliance while a third group had a combination of biteplate and headgear. It was found that removable functional appliances had no white spot lesions developed on the molar teeth and perhaps allow for better remineralization[39]. While such finding could be promising for removable appliances, the conclusion cannot be used to claim that clear removable aligners would have no effect on the decalcification of the teeth since such appliances are of completely different design as compared to the Bionator or other Class II functional appliances[39].

Furthermore, measuring white spot lesions could be done in several ways. The most common methods are visual inspections and digital photography. Each method has its advantages and disadvantages. Digital photographs have the following advantages over visual inspection[40]:

1) Quick and efficient

2) Provide permanent records hence reproducible

3) Possible masking of patient details to eliminate/reduce potential bias

4) Images taken by several operators can be examined by one only and vice versa

5) More versatile than visual exam and images can be digitised for computer analysis.

Drawbacks, on the other hand are[40]:

1) Different recording of details compared to naked eyes which may result in overestimation

2) Difficult to standardise the image-taking procedure

3) Expenses.

The use of digital imaging in the analysis of WSLs has been proven to be both valid and reliable method[40-42]. In addition, Livas *et. al.* (2008) has concluded that images could be used as a reproducible and reliable method for quantification of white spot lesions[43]. In their study, they considered taking photographs at two different angulations 90 degrees and 110 degrees of in-vitro demineralized incisors. Analysis of the lesions was conducted by two examiners using image-processing-software. Despite looking at two angles by two observers, the reproducibility of the measurement was good overall[43].

One of the shortcomings of image analysis is magnification errors that results from taking the pictures at different angulations or the use of different cameras and settings. In order to measure the extent or the surface area of the lesions and in the same time take into the consideration the issue of magnification, one could measure it as a ratio. Therefore, the surface area of the lesion could be outlined using an image-processing software and then divided by the outlined surface area of the entire buccal surface of the tooth. Such method has been investigated and proven valid and reproducible by Chapman *et. al.* in 2010[44].

Rationale

Many orthodontic products and appliances are released in the market each with year without enough clinical data or trials that test their efficacy which is quite problematic for both the practitioner as well as the patients[45]. Invisalign® is one of these products which lacks enough randomized trials that investigate its treatment outcomes and side effects in comparison to other appliances. Having said that, there has been no study that has compared the development white spots between clear aligners and fixed braces including conventional and self-ligating brackets. As such, it is imperative to conduct a prospective clinical study to find an evidence-based orthodontic treatment protocol, among the different appliances, that leads to predictable outcome in terms of having straight teeth with no or very minimal white spot lesions.

Null Hypothesis

There is no difference in the incidence and the severity of white spot lesions among clear aligners, self-ligating brackets and conventional brackets.

Specific Aims

The following aims will be studied to compare the three different appliance systems:

SA-1: To measure the incidence of WSLs in the three different groups and compare it among each other

SA-2: To measure the severity of WSLs in the three groups by measuring the extent/size of the lesions and compare it among each other

SA-3: To evaluate whether or not there is a correlation between Gingival, Plaque and Bleeding Indices and WSLs. Note that the indices were measured in the first part of the study that was conducted by Dr. Agarwal.

MATERIAL AND METHODS

Study Design

This study is considered as part II 'or a continuation' of a recent randomized clinical study conducted in the Division of Orthodontics, Department of Craniofacial Sciences, at the University of Connecticut Health Center by Dr. Sachin Agarwal. The project directed by Dr. Agarwal was approved by the Institutional Review Board of University of Connecticut Health Center (IRB# 12-025-2). His part in this prospective randomized clinical trial was to make a comparison of Root Resorption, Microbial Colonization and Periodontal Status between Clear Aligners (Invisalign®), Self-Ligating Braces and Conventional Braces. During his part, he collected the image data at two different time points. These data will be evaluated by H.A. in this part of the study to compare the incidence of White Spot Lesions between the same three groups.

It is worth noting that the following parts of the material and methods are taken directly from Dr. Agarwal Thesis as the sample used here is exactly the same.

Sample Size and Power Analysis: (As stated in Dr. Agarwal Thesis)

From previous studies, it was inferred that a mean colony forming unit (CFU) difference of approximately one log (standard deviation (SD) = approximately 1) would result in a clinically significant increase in *S. mutans* counts. Therefore the sample size of 15 patients per group, at $\alpha = 0.05$, yielded a statistical power of approximately 0.80 for this study. To account for a 10-20% patient drop out and data loss due to other unavoidable circumstances, we enrolled 60 patients for this study.

Patient selection (As stated in Dr. Agarwal Thesis)

The patients were selected from the Division of Orthodontics, Department of Craniofacial Sciences, University of Connecticut Health Center. The following were the inclusion criteria;

1. Nonextraction treatment plan.

2. There should be less than 8mm of anterior crowding.

3. Patients should have all permanent teeth present, except third molars.

4. Demonstrable ability to maintain adequate oral hygiene.

5. Show optimum dental health without immediate need for restorations.

The following were the exclusion criteria:

1. Skeletal anterior-posterior discrepancies between the maxilla and mandible (ANB $\geq 5°$).

2. Centric relation (CR) - Centric occlusion (CO) discrepancies of greater than 3 mm.

3. Anterior or posterior open bites.

4. Patients who are pregnant, diabetic or using mouth rinses or interacting medications, including antibiotic therapy.

5. Presence of impacted teeth.

6. Presence of pre-treatment white spot lesions.

7. Presence of active periodontal disease as evidenced by attachment loss.

The patients who fulfilled the above criteria were randomly assigned to one of the treatment groups outlined below:

• Group 1 (G1): Patients receiving treatment with clear semi-elastic polyurethane aligners.

• Group 2 (G2): Patients receiving treatment with self-ligating brackets.

• Group 3 (G3): Patients receiving treatment with conventional pre-adjusted edge wise brackets.

At the patient's regular records appointment, the primary investigator (S.A.) screened the patient to evaluate if the patient satisfied the inclusion criteria for the study. Upon satisfaction of the inclusion criteria, informed consent was signed by the subject. If the subject was under the age of 18, informed consent was also obtained from the parent.

Randomization Sequence and Allocation (As stated in Dr. Agarwal Thesis)

The patients who fulfilled the above criteria were randomly assigned to one of the treatment groups outlined below:

- Group 1 (G1): Patients receiving treatment with clear semi-elastic polyurethane aligners known as Invisalign® (Align technology, Santa Clara, California).
- Group 2 (G2): Patients receiving treatment with self-ligating brackets. (Carriere Self- Ligating Bracket, Carlsbad, CA).
- Group 3 (G3): Patients receiving treatment with conventional pre-adjusted edge wise brackets (PEA).

Randomization sequence was generated by using a PC based software "Random Allocation Software". Random sequences in blocks of 15, 9, 6 and 3 were generated to ensure even distributions of the patients in all the 3 groups. A second set of random sequence was generated in blocks of 2, 4, 6 and 8 for randomization of right or left side. So, each patient was allocated to one group i.e. G1, G2, G3 and either right side or left side. For example, patient number 34 was G2 left side, so the patient was allocated to the self-ligating group and his/her maxillary left lateral incisor and second premolar was used for clinical and radiographic examination.

The randomization sequence was held by the supervising faculty member. Once the patient/parent agreed to be a part of the study and signed the consent form, the supervising faculty member disclosed to which group that particular patient was assigned.

Patient De-identification and Decoding (As stated in Dr. Agarwal Thesis)

All research data were identified by unique identifier (Patient1, Patient 2 …) that contained no protected health information (PHI). Specifically, all data collected from the experiments were not associated with patient's name, medical ID number, or any other identifier which could readily identify the patient. All patients' data that were gathered were transferred immediately to a secure database where the data could be identified only by unique identifiers that were created for each patient. The list that coded the unique identifiers to the patient names was maintained in a secure, locked location that was separate from the data and could be viewed only by approved, qualified research personnel. At the completion of the study, the list was decoded to analyze the data. All electronic data were stored in a password protected computer with backup file which could be accessed only by the principal investigator, primary investigator (SA) and research advisors.

Data Collection and Evaluation procedures

Measuring white spot lesions will be carried out using digital color photographs that are taken at two different time points. Pretreatment pictures (T0) will be taken from the record visit of the patients while intra-treatment pictures (T2) will be taking after 18 months of the treatment unless the patient is de-bonded earlier to 18 months. There are no pictures after 9 months which represent T1. The comparison is, therefore, only between T0 and T2. In order to reduce the risk of the bias when analyzing the data, the picture should only show the teeth without any metal or resin attachment. However, it would not be practical to remove the braces or the resin attachments of the Invisalign® from the entire dental arch to take a picture while the patient is still in treatment as this may have compromise the treatment. As such, the measurement of lesions will be carried out on only maxillary lateral incisors since they show the highest prevalence of white spot lesions especially on the buccal tooth surface at the periphery of the bracket as reported in the literature. Computer generated random numbers

randomized the right and the left sides of the maxilla for selecting the experimental side. This is similar to first part of the study where the lateral incisor was used to represent the anterior maxilla for root resorption.

As mentioned earlier, two intra-oral pictures would be taken. The first is at T0 where the dentition have no attachment and the second capture is at T2 after removing the bracket or the resin attachment from the tooth in question. The T0 and T2 pictures will then be cropped to show only that tooth. These two picture would be saved in a data folder that pertains to each unidentified patient. Each picture would then be assigned a random number for further evaluation later on. For example, patient number 23 could receive number 1 for the T2 picture and number 163 for the T0 picture. In other words, the value of the number of the picture could neither indicate the patient group nor the time when photo was taken.

After gathering all the pictures for the three groups, the cropping and number assignment procedures were performed by an orthodontic fellow A.A. to reduce the risk of bias when evaluating the images by the principal evaluator of this part of the study, H.A. The role of the evaluator H.A. is to project the images in a random fashion on a computer screen and evaluate whether or not each tooth has White Spot Lesion. The software Wildbit Viewer (64bit, Version 6.3 Final, Copyright Marko Hietanen) was utilized for that purpose. Once identifying those teeth with WSL, the random number of each picture was then inserted in a new Excel sheet to allow for measuring the size of the lesion in the following step of the study.

The principal evaluator (H.A.) would have to measure the size of the lesions at two separate time points in order to assess intra-rater reliability. The difference between the two points of time should be at least one week. Once H.A. completes all the measurements, he would then assign another numbers for all those images with WSLs so that the secondary evaluator (A.A.) measures the same lesions in order to assess the inter-rater reliability for measuring the size of the WSLs.

UNIT OF ANALYSIS AND OBSERVATION

Specific Aim #1: Measuring the incidence of WSLs

The presence of a white spot lesion will be inspected using a modified version of the 'Gorelick White Spot Lesion Index'[11]. The original version of the index is shown in Figure 1 which indicates different level of severities of WSLs.

The modified version, on the other hand, combines the categories 1 and 2 into one group such that it would be used to quantify the number, hence the incidence, of white spot lesions developed and not the severity as the latter will be evaluated using a different method (Figure 2). The number of patients with WSLs at T2 as compared to T0 would be calculated to measure the incidence of WSLs in each group and to compare the incidence between the groups.

Specific Aim #2: Measuring the Severity (Surface Area) of WSLs

In order to measure the severity or the extent of the WSLs since it is one of the aims of the study, the ImageJ software will be utilized. The idea of it is that the surface area of the lesion can be delineated and then calculated as a ratio in relation to the entire tooth surface area to account for any magnification errors due to different image sizes. This method has been used before in a study which also reported its reliability (pct 43).

The reliability of this method was also measured in this present study as mentioned earlier. The principal examiner H.A. would repeat the measurement twice for intra-rater reliability testing and his measurements would also be compared to those by the secondary evaluator A.A. for inter-rater reliability testing. The pictures in Figure 3 show how both the lesion and the entire tooth are outlined. Once the surface area of the lesion was outlined, the software will automatically calculate and tabulate it. The surface area of the entire tooth was also delineated and measured by the software which would in turn divide the two values by

each other in order to give the ratio of the lesion surface area in relation to that of the whole crown.

Once all the ratios are computed, the severity of the lesions could then be compared between the groups. In addition, based on the extent of the lesions, the patient with white spot lesions (WSLs) could be categorized into one of three groups. Should the ratio of the lesion be equal or less than a third (33.3%), the patient would have been placed into Category I (Mild WSL). A ratio between >33.3% and =<66.6% would score category II which is the Moderate WSL and a ratio >66.6% would be of a 'Severe' form of WSL hence Category III. Obviously those without any WSL would be in Category 0.

Evaluating the extent or the severity of the lesions amongst the group would also allow a possibility of quantifying how severe the WSLs that are caused by each appliance. In addition, a comparison between all the three groups could be made in terms of the number of patients in each category.

Specific Aim #3: Measuring the Correlation between Gingival, Plaque and Bleeding Indices and White Spot Lesions

As explained by Dr. Agarwal in his thesis which discuss the first part of this study, periodontal measurements including plaque index, gingival index and bleeding on probing Index were recorded specifically for the maxillary lateral incisor as a representative tooth for the anterior segment. Measurements were taken at three different time intervals:

T0: Before treatment

T1: 9 months after commencement of treatment

T2: 18 months of active orthodontic treatment or debonding, whichever is earlier.

Since the Data of WSLs are only taken at T0 and T2, the statistical correlation would only be measured at those time points. For further details on how the aforementioned periodontal indices were measured, kindly refer to Dr. Agarwal thesis.

Statistics

Data were statistically analyzed using a commercially available statistical software package SAS 9.4 (SAS Institute Inc, North Carolina, USA). The incidence change from T0 to T2 is a categorical measure. The frequencies and proportions were summarized. To assess whether the incidence change is significantly different among groups, we excluded the patients with incidence at baseline and Pearson Chi-square test was performed. The lesion surface area (size) change is a continuous measure. Means, Standard Deviation, Median, Range and other descriptive statistics were summarized. Since histogram showed that the data distribution of size change severely deviated from normality, non-parametric statistic tests were performed. These include Wilcoxon signed-rank test for evaluating the lesion surface area changes within the groups and Kruskal-Wallis test for comparison across the groups. Lastly, The Spearman correlation coefficients between lesion size change and the changes in gingival architecture (Gingival Index), appearance of plaque (Plaque Index), and bleeding pattern (Bleeding on Probing Index) were measured. A two-sided α level of significance of 0.05 was used in statistical tests.

Reliability Test

Considering the presence or absence of a lesion as binary outcome such as absence of lesion is ‘no’ and presence of it is ‘yes’, then kappa coefficients (κ) were used to measure between- and within- rater agreement.

When it comes to the measurement of the surface area of the lesions, then intra-class correlation (ICC) for the non-zero size data was used to evaluate between- and within- rater reliability.

Results

Pretreatment Baseline Demographic Comparisons

The demographics of the study sample; i.e., the patient age and sex, are reported in Table 1. There was a significant difference in the ages of the three groups (p = .02) with G1 being significantly older (21.44 SD 11.62) when compared to G2 (14.82 SD 4.26) and G3 (14.47 SD 3.99) (Table 1), and there were more males than females in the three groups. There was no significant difference for the treatment intervention duration for the three groups between the time point T2-T0 (p = 0.20) (Table 1).

Measuring the incidence of White Spot Lesion in the groups

In group 1, 29% of the patients developed WSL at T2 while 41.7% remained lesion-free from T0 to T2. In group 2, approximately 44% of the patients had WSL at T2 while 25% of them stayed lesion-free from T0 to T2. In group 3, roughly 47.4% of the patients developed WSL at T2 whereas 42% had no lesion at T2. The addition of both percentages of each group is less than 100% because there patients who started with WSL and remained with it. If we consider the entire sample size, then the incidence of WSL, regardless of the appliance type, is about 39% (Table 2).

The incidence of WSL was measured as a percentage of those patients who developed new lesions within each group at T2 as compared to T0. In order to ensure better measurement, those patients with an existing lesion(s) at the baseline T0 were excluded and the results are shown in Table 3. For Group 1, 2, 3, the percentage of patients who change from lesion-free at T0 to having lesion(s) at T2 were 41.18% , 63.64%, and 52.94%, respectively. The P-value from exact Pearson Chi-square test is 0.5627 (> 0.05). Therefore, there is no enough evidence for significant group differences in lesion incidence (Table 3).

Measuring the Surface Area (size) change of White Spot Lesion in the groups

Difference in the WSL Surface Area (SA) were calculated by subtracting the Surface Area at T0 from size at T2. (ie. Diff_SA= $Size_{T2}$- $Size_{T0}$). P-values were from Wilcoxon signed-rank test, which tested the change from T0 to T2 within groups. All P-values were <0.05, indicating that the size change from T0 to T2 were all significant within each group (Table 4).

Considering that the data distribution of 'differences in surface area (size) of WSLs' is severely deviated from normality, Kruskal Wallis test was performed to the test the SA change across the groups. The P-value is 0.2763 (> 0.05), indicating that the size change doesn't significantly differ among the groups (Figure 4).

Categorizing the WSLs into mild, moderate and severe based on the surface area and measuring the change of categories from T0 to T2

The surface area of a WSL is measured as a ratio in relation to the total surface area of the teeth. As such the lesion size or SA could vary from zero to 100%. Based on the percentages, the patient could be categorized into category C0, C1, C2, or C3 if the WSL ratio is 0%, between 0.1 to 33%, 33.1% to 66%, or 66.1 to 100% respectively.

Data analysis showed that few patients reached the Category of Moderate (C2) and none reached the Severe Category (C3). There were 2 cases of Moderate Category at T2 in total. 1 patient in Group1 and Group3 each changed from None to Moderate Category. For patients started from none at T0, 64% (7/11) of patients in Group 2 moved from none to minor or moderate. The percentage was 53% (9/17) in Group 3 and 41% (7/17) in Group 1 (Table 5).

Measuring the Correlation between Gingival, Plaque and Bleeding Indices and White Spot Lesions:

The Spearman correlation coefficients between lesion size change and the changes in gingival architecture, appearance of plague, and bleeding pattern were 0.087, 0.167 and 0.0032, respectively. The correlation coefficients are not significantly different from zero, as the P-values were 0.51, 0.21 and 0.98 respectively (all P values > 0.05). Therefore, there is no linear relationship between the lesion size (SA) change and the changes in gingival architecture, appearance of plague, and bleeding pattern (Tables 6.1, 6.2 and Figure 5).

Evaluating the reliability for intra- and inter-rater measurements:

A. Intra-rater (H.A.) reliability test for measuring the presence or absence of lesions (Binary Y/N outcome):

For T0 data, the observed agreement rate within rater-H.A. was 96.6%. Cohen's kappa coefficient was 0.91 with a 95% confidence interval from 0.78 to 1, indicating good to excellent agreement within rater-H.A. (Tables 7.1 and 7.2)

For T2 data, the observed agreement rate within rater-H.A. was 96.6%. Cohen's kappa coefficient was 0.93 with a 95% confidence interval from 0.83 to 1, indicating excellent agreement within rater-H.A. (Tables 8.1 and 8.2)

B. Intra-rater (H.A.) reliability test for measuring the surface area of the lesions:

A high degree of reliability was found within Rater 1 for T0 size data. The ICC was 0.95 with a confidence interval from 0.86 to 0.98. (Table 9.1)

A high degree of reliability was found within Rater 1 for T2 size data. The ICC was 0.97 with a confidence interval from 0.95 to 0.99. (Table 9.2)

C. Inter-rater (H.A. and A.A.) reliability test for measuring the presence or absence of lesions (Binary Y/N outcome):

For T0 data, the observed agreement rate between rater H.A and rater A.A. was 93.2%. Cohen's kappa coefficient was 0.82 with a 95% confidence interval from 0.65 to 0.99, indicating good to excellent agreement between the two raters (Tables 10.1 and 10.2)

For T2 data, the observed agreement rate between rater H.A and rater A.A. is 98.3%

Cohen's kappa coefficient is 0.96 with a 95% confidence interval from 0.89 to 1, indicating excellent agreement between both raters.

D. Inter-rater (H.A. and A.A.) reliability test for measuring the surface area of the lesions:

A high degree of reliability was found between rater H.A. and rater A.A. for T0 size measurements. The ICC was 0.98 with a confidence interval from 0.96 to 0.99 (Table 12.1).

A high degree of reliability was found between rater H.A and rater A.A. for T2 size data. The ICC was 0.98 with a confidence interval from 0.96 to 0.99.

Discussion

Sample Selection, Material, and Methods:

Prior to discussing the results findings, it is important to clarify some points related to the material and methods of this study. Perhaps the reader of this study would wonder why is it only one tooth that has been investigated, that is the maxillary lateral incisor. Usually, studies in the literature look at more than one tooth. This study differs to those previously conducted in the fact that it is a prospective randomized clinical trial in which the evaluator would be blinded when it comes to assessing the outcomes. As the objective was to assess the incidence of WSL during the treatment and as blinding was a principal part of the assessment methodology then it was necessary to remove the appliance prior to the evaluation or to taking the picture of the teeth. As such, it would not be practical to take the entire braces out just to take a picture and then rebond the entire dentition and perhaps it is unethical as it might delay the patient treatment unpurposefully. Therefore, one tooth was selected to represent the mouth which is the maxillary lateral incisor. This tooth has been selected because it is found to be the most susceptible tooth to both root resorption (as per the first part of the study) and white spot lesions. According to Gorelick *et. al.*, Artun *et. al.*, Øgaard, Chapman *et. al.*, Julien *et. al.*, and Lucchese *et. al.*, the maxillary lateral incisor has the highest incidence or prevalence of white spot lesion[11,9,18,44,46,47].

With regards to the method used to evaluate the decalcification of the enamel tooth surface, several authors have used intraoral color slides before, during, or after orthodontic treatment[11,14,16,17,48-54]. Another study by Willmot et al. (2000) reported that converting the color slides into digital images is still a reliable method to measure WSLs. With the introduction of digital camera into the dental field, multiple studies have found that direct digital camera images are as accurate, reproducible, and valid as captured slides[17,40-42,49,51,53,56]. In the present study, intraoral photographs taken by digital cameras were used to evaluate the formation of white spot lesions.

It is important, however, to understand that digital cameras might capture the details of teeth differently as compared to naked eyes. Reflections from the commonly used ring flash in orthodontics might complicate the evaluation of white spot lesion. Figure 6 is an example of how flash light reflection may result in false positive white spot lesions[57,58].

Moreover, digital photographs not only help in evaluating the presence or absence of white spot lesions but also can help in measuring the extension of such lesions. Several methods and indices have been reported in the literature. Gorelick et al. (1982) reported a semi-quantitative classification system which scores the size and the severity of WSL[11]. Årtun and Brobakken (1986) also described a quantitative evaluation system that compute the number of lesions around the brackets but not the extent of them[9]Banks and Richmond (1994) described another system in which areas of decalcification were localized[59]. Nevertheless, the latter two methods are not commonly reported and used in the literature. Gorelick's method is more popular and is usually implemented in white spot lesion researches. The index reported by Gorelick can assess both the presence and absence of WSL as well as the severity of it. It has 4 scores from 0 to 3. A score of 0 means no white spot lesion has formed, a score of 1, 2, or 3 means that a slight, excessive, or excessive and cavitated WSL has formed respectively (Figure 1). This index was implemented with a modification however in this study as shown in Figure 2. In other words, the index was used only to evaluate the presence or absence of white spot lesions on the teeth surface. The severity was evaluated differently in the present study as described by Chapman et al. as mentioned earlier in the methodology section of this report (Figure 3)[44]. This method is selected as to take into consideration the magnification and angulation issues that are associated with the taken images. By this method, the total surface area of a lesion could be measured in relation to the entire surface area of the labial surface of the tooth and then computed as a ratio. Based on the calculated ratios, the lesion could be

classified as either mild, moderate or severe which is a better classification than that reported by Gorelick since it lacks the moderate category.

Intra-examiner reproducibility and inter-examiner reliability

For the presence or absence outcome of a lesion (Lesion absence =0 or Lesion presence>1), we used kappa coefficients (κ) according to Landis and Koch to measure between- and within- rater agreement[61]. For a thorough interpretation of the kappa coefficients, please refer to the appendix[61]. Excellent agreement within rater H.A. was found for evaluating the presence or absence of WSL at both T0 and T2. The agreement rate was about 96% at T0 and T2 within the same first rater. In addition, the observed agreement rate between rater H.A. and rater A.A. is 93.2% and 98.3% at T0 and T2 respectively.

For surface area measurements data, we used intra-class correlation (ICC) according to Cicchetti to evaluate between- and within- rater reliability[62]. For thorough interpretation of ICC, please refer the appendix. A high degree of reliability was found within Rater H.A. at T0 and T2. Additionally, a high degree of reliability was found between rater H.A. and rater A.A. for T0 and T2 surface area measurements. The ICC was 0.98 with a confidence interval from 0.96 to 0.99 for the two time points.

Results and Findings:

It has been well documented in the literature that conventional orthodontic treatment can and will cause some sort of either permanent or transient side effects on the periodontium and dentition. Gingival and periodontal inflammation are common soft-tissue side effects on orthodontic treatment that usually lead to gingival overgrowth and bone loss especially when the patient has very poor oral hygiene. Dentally, the teeth may undergo root resorption and decalcification that appears as white spot lesions on the enamel surface. Oral hygiene maintenance has to be very meticulous for patients with braces otherwise the plaque accumulation and retention can happen faster than those without braces which in turns

increases the risk of side effects. Dental plaque on enamel surfaces acts as scaffold for multiple infective agents which all collectively can result in tooth surface demineralization and subsequent caries as well as periodontal diseases. Plaque build-up can be affected easily by the presence of different appliances in the mouth. For example, the presence of a straight wire perhaps allows easier cleaning when compared to the use of multi-loop wires and cantilevers[62]. Similarly, the method of ligation might affect the plaque level on the teeth surface[62]. The incidence of White Spot Lesions (WSLs) has been well-reported in the literature. On the other hand, during the search process for this research, very few studies were found that compare the incidence of WSLs between conventional braces and self-ligating braces and none were found that compares the former with clear aligners. For this reason, it was imperative to evaluate the occurrence and incidence of white spot lesions with each appliance and compare them to understand the differences, if any, among them in regards to this particular outcome. The present study is prospective randomized clinical trial that compares the incidence of white spot lesions across the three different appliances in order to find a sound evidence-based orthodontic treatment protocol that leads to predictable outcome in terms of having straight teeth with no or very minimal white spot lesions.

A base line statistical analysis was executed to evaluate whether the three groups were similar at the beginning of treatment (T0) in terms of the demographics. Despite the randomization of the patient sample, significant differences were present at the baseline for the mean age in all groups. The mean age difference was higher with the Clear Aligner (Invisalign®) group as compared to conventional and self-ligating groups. This could be attributed to the numerous dropouts after the initial screening and allocation (Consort Flow Chart, Appendix). Such dropouts could be explained by parental thoughts that their children might not be responsible enough to wear the aligner for the required minimum of 22 hours per day.

The incidence of WSL from T0 to T2 was measured and the frequencies and proportions were reported in table 2. Among 24 patients in Group 1, 10 patients (41.67%) remained lesion-free from T0 to T; 7 patients (29.17%) changed from lesion-free to having lesion(s); 7 Patients (29.17%) remained to have lesion(s). In group 2 and 3, approximately 44% and 47.4% changed from having no lesion at T0 to having a lesion at T2. Considering the entire sample regardless of the appliance type, orthodontic treatment caused white spot lesion in 39% of the patients. These measurements are calculated by including all the patient sample even those who started with white spot lesion before the treatment.

In order to correctly assess whether the incidence change is significantly different among groups, we excluded the patients with incidence at baseline and Pearson Chi-square test was performed and the results are shown in Table 3. The incidence of WSL was measured as a percentage of those patients who developed new lesions within each group at T2 as compared to T0. For Group 1, 2, 3, the percentage of patients who change from lesion-free at T0 to having lesion(s) at T2 were 41.18%, 63.64%, and 52.94%, respectively. The P-value from exact Pearson Chi-square test is 0.5627 (> 0.05). Therefore, there is no enough evidence for significant group differences in lesion incidence (Table 3). The overall incidence of WSL at T2 regardless of the type of the appliance is 52.59%. This outcome is in agreement with many studies that reported similar values of white spot lesions during or after orthodontic treatment[9,11,12,57,63]. Perhaps one the most quoted study is conducted by Gorelick in 1982 in which he found that approximately 50% of the subjects had an increase in the number of white spot lesions with fixed braces[11,12]. The findings are also consistent with those found by Stratemann and Shannon who reported 58% of tooth surface decalcification[63]. Another similar finding to our result is that document by Artun et. al. in 1986[9]. They reported WSL prevalence of 59% in patients with multibonded orthodontic appliances[9]. Enaia *et. al.* (2011) found that WSL incidence is about 61% immediately after debonding or 1 week prior to it[57].

Some studies have found different incidences of white spot lesions as compared to what we found. Chapman et. al. found that white spot lesions occur in the anterior maxillary teeth by about 36%[44]. Lucchese reported prevalence of WSLs of 29% in maxillary lateral incisor area[47]. Julien et. al. stated that 23% of patients developed WSLs during orthodontic treatment[46]. Tufekci et al found that the percentage of WSLs was 38% after six months in braces and this increased to 46% after reaching twelve months in braces[64]. The latter is however similar to our findings after 18 months in braces. Øgaard (1989) found that the prevalence of WSL is only about 11% after 5 years of fixed appliance therapy[18] while Tuncay *et. al.* reported prevalence of 14.3% of mild white spot lesions in patient with clear aligner therapy in teenage patients[65]. The last two mentioned studies reported incidence rates that totally disagree with our outcomes as compared to both fixed and removable appliances.

In this study there was no significant different between the types of appliances in terms of the incidence of white spot lesions. In other words, fixed and removable Invisalign® appliances have comparable incidence of WSL. This is similar to what was found by Buck *et. al.* 2011[34]. Buck reported that there is no statistical significant difference between conventional and self-ligating brackets, however; the prevalence was only 14% which is not in agreement with our findings[34]. Possibly the difference is attributed to the very small sample size used in their pilot study[34]. Another similar study by Polat *et. al.* (2008), which compares the formation of white spot lesion between conventional and self-ligating brackets, found that there was no significant difference in between the two groups[66]. Their reported percentages of patients having WSL were 23% and 25% for the self-ligating and the conventional brackets groups respectively both of which are almost half of what was found in this present study[66].

As reported earlier, there was no difference between the two fixed appliances and the removable ones in relation to the incidence of WSLs. This finding is in contrast with that found

by Alexander (1993) who found an increase in the white spot lesions with fixed appliances as compared to patients who are treated with removable functional appliances[39]. This study however compared patients wearing headgear to another group wearing Bionator appliance. The headgear group was considered the fixed appliance group due to the presence of molar bands on the maxillary first molars. This may explain the difference in the findings between the two studies.

Moreover, in the present study, difference in the WSL Surface Area (SA) were calculated by subtracting the Surface Area at T0 from size at T2 (ie. SA Difference= $Size_{T2}$-$Size_{T0}$). The change in the surface area from T0 to T2 was statistically significant within each group (Table 4). On the other hand, such changes when compared between the entire three groups, then the statistical tests showed insignificant results (Figure 4).

On average white spot lesions covered 6.6%, 11%, 9.3% of the entire facial enamel surface of the teeth in Group 1, Group 2 and Group 3 respectively. If we consider the entire sample with disregard to the appliance type, then the average surface area of WSL during orthodontic treatment is 8.96% of total surface area of the facial enamel surface. These findings are in concordance with the result of Chapman et. al (2010) who found that The average WSL covered 9.8% of the total facial surface of the affected tooth[44]. As mentioned earlier, Chapman et al. found that WSL formed in 36% of the patients. 22% of the them had WSL with surface area of less than 10% while the other 14% had WSL that is more than 10% in terms of the surface area[44]. In other words, the aforementioned study divided the patients into two categories of WSL yet the division is not equal as the second division could range anywhere between 10.1% to 100%.

However, this present study categorized white spot lesions into 4 categories based on the surface area ratio. As such the lesion size or surface area could vary from zero to 100%. Thus, the patient could be categorized into four categories C0, C1, C2, or C3 if the WSL ratio

is 0%, between 0.1 to 33%, 33.1% to 66%, or 66.1 to 100% respectively. C0 basically means lesion does not exist, C1 means a mild lesion exists, C2 equals to an existence of a moderate lesion while C3 means a severe white spot lesion has formed. Considering these categories, it was found that all the patient who started with no WSL at T0 and developed WSL at T2 are in the mild category except 2 patients. While these two patients were in located in the moderate category, they are not from the same group. One of them is from G1 and the other is from G3. No patient in G2 was found in the moderate category and no patient in the whole three groups was found in the severe category. Mathematically, for patients started from none at T0, 64% (7/11) of patients in Group 2 moved from none to mild category only while 53% (9/17) in Group 3 and 41% (7/17) in Group 1 moved to mild or moderate categories collectively (Table 5). In comparison to our findings, Tuncay et. al. (2013) found that 3 of 336 teeth (0.9%) changed to moderate WSL and another 3 teeth changed to severe WSL while the 14.3% of them had mild WSL and the majority (75.6%) had no lesion[65]. Enaia *et. al.* also reported on the changes in the severity of WSL in their study. They found that immediately after treatment, most patients (63.3%) had mild lesions, but the remaining were affected severely[57]. The evaluation system used in their report is slightly different however since the categories were mild, severe, and severe with cavitation; what they found to be severe could be considered either moderate or severe in our measurement system.

In the first part of this study which was conducted by Dr. Agarwal, it was found that Gingival Index and scores increased from T0 to T2 for all the three groups in the lateral incisor region with a statistical significance within each group. Post-hoc analysis however revealed that such change was statistically different between G1 and G2 ($p = 0.00$) and between G1 and G3 ($p = 0.022$), whereas there was no significant difference between self-ligating brackets and conventional brackets groups ($p = 0.566$). Our observation was in accordance to the results published by Pejda et al.[67]

In addition, it was also found that plaque index and scores increased from T0 to T2 for all the three groups in the lateral incisor region with a statistical significant difference within each group. Post-hoc analysis however revealed that such change was not significant among the three groups.

The Clear Aligner group showed a significant decrease in the bleeding on probing pattern (-.13 SD .992) for lateral incisor region from T0 to T2. On the contrary, the bleeding on probing (BOP) showed a statistically significant increase in both G2 (.80 SD 1.207) and G3 (.47 SD 1.429) from T0 to T2 indicating an increased tendency for the gums to bleed. Considering a comparison among the three groups, the change in the bleeding index from T0 to T2 was significantly higher in Clear Aligner group as compared to the Self-ligating group only. These observations are contrary to Ristic et al.[68] who reported a decrease in periodontal parameters after 3 months of conventional fixed appliance therapy and Karkhanechi et al.[69] who also compared Clear Aligners to conventional appliances for a duration of 12 months and reported that periodontal indices in the fixed buccal appliance group reached maximal values 6 months after placement of appliances, followed by a decrease at 12 months, contrary to our observations of an increase in periodontal parameters from baseline values. However, they also reported less plaque accumulation with removable aligners at 6 and 12 months when compared to fixed buccal appliances, similar to our observation.

The reason for recalling such finding because a correlation test was performed in this present study to evaluate if any correlation exists between the increase in WSL surface area and the changes in the status of the periodontal incides. Nonetheless, no linear relationship between the lesion size (SA) change and the changes in gingival architecture, appearance of plaque, and bleeding pattern was found (Figure 5, Table 6).

Study Limitation

Perhaps the largest limitation of this study is the lack of a standardized protocol of image taking technique. There were no specifications on the camera type, lens type, settings prior capturing an image, angle at which an image should be taken, and lightening conditions.

The sample size was relatively small in relation to other studies on white spot lesions. Those studies were retrospective however. This present study was prospective and power analysis was done in the first part of the study nonetheless it was based on a different aspect of the study.

Conclusions

Conclusions

Based on the findings of this study. The null hypothesis is accepted as there is no difference in the incidence and the severity of white spot lesions among clear aligners, self-ligating brackets and conventional brackets.

There was a significant difference in the ages of the three groups with G1 being significantly older than the other two groups and there were more males than females in the three groups.

The percentages of patients who developed white spot lesion are 41.18%, 63.64%, and 52.94% in group 1, group 2, and group 3 respectively.

The increase in the surface area of white spot lesions at T2 was significant per each group individually.

Comparison between the three groups in terms of the changes in the surface area of the developed white spot lesions yielded no statistical difference between them.

In general, almost all white spot lesions that develop during orthodontic treatment are of mild nature.

Based on the reliability tests, digital photography is an adequate method to evaluate the dimensions of the lesions and the existence. In other words, they are diagnostic.

Despite the increase in the gingival index, plaque index, and bleeding on probing index status, there was no correlation between them and the change in the dimension of WSLs.

FIGURES

Figure 1: Gorelick White Spot Lesion Assessment Index

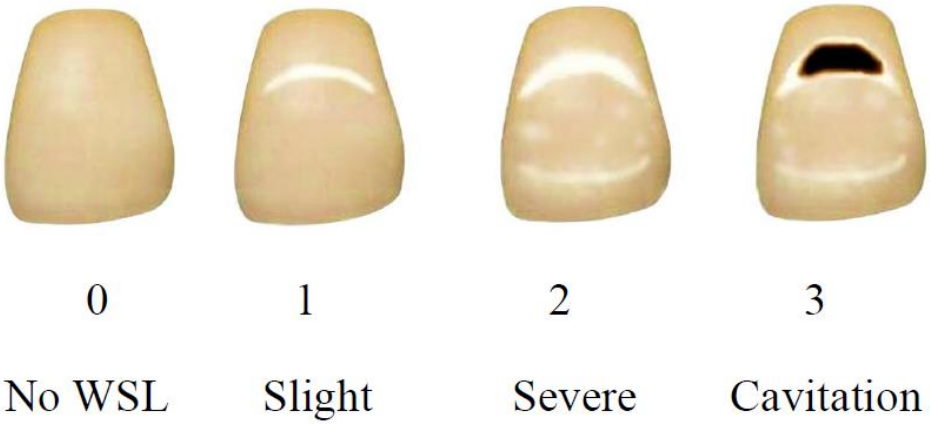


Figure 2: A modified version of Gorelick WSL Index as per the present study

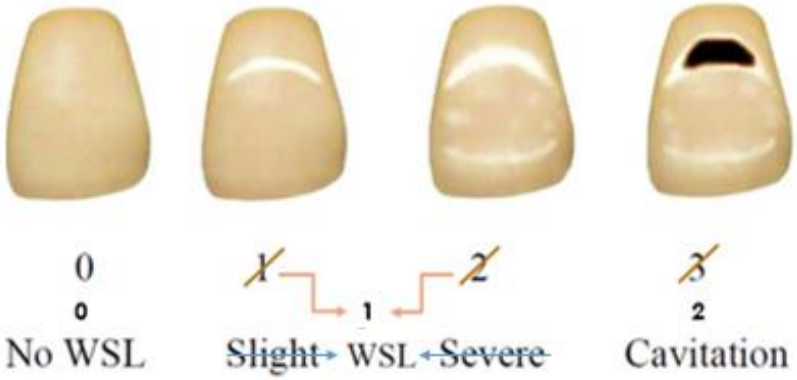
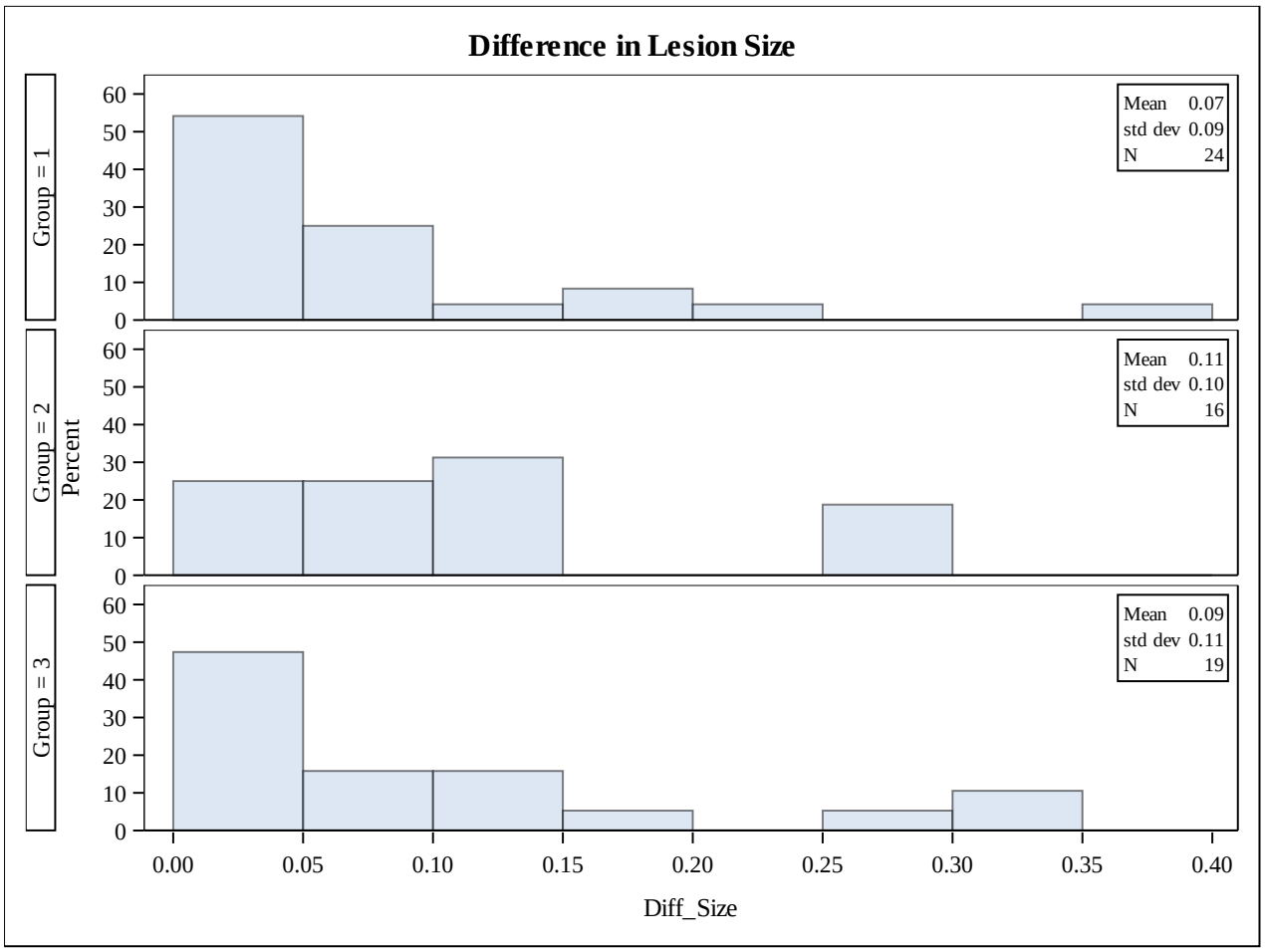


Figure 3: Example of ImageJ Software usage

Figure 4: Difference in Lesion Size (Surface Area/SA)



Kruskal-Wallis Test	
Chi-Square	2.5723
DF	2
Pr > Chi-Square	0.2763

Figure 5: Scatter Plot Matrix for Spearman Correlation Coefficients

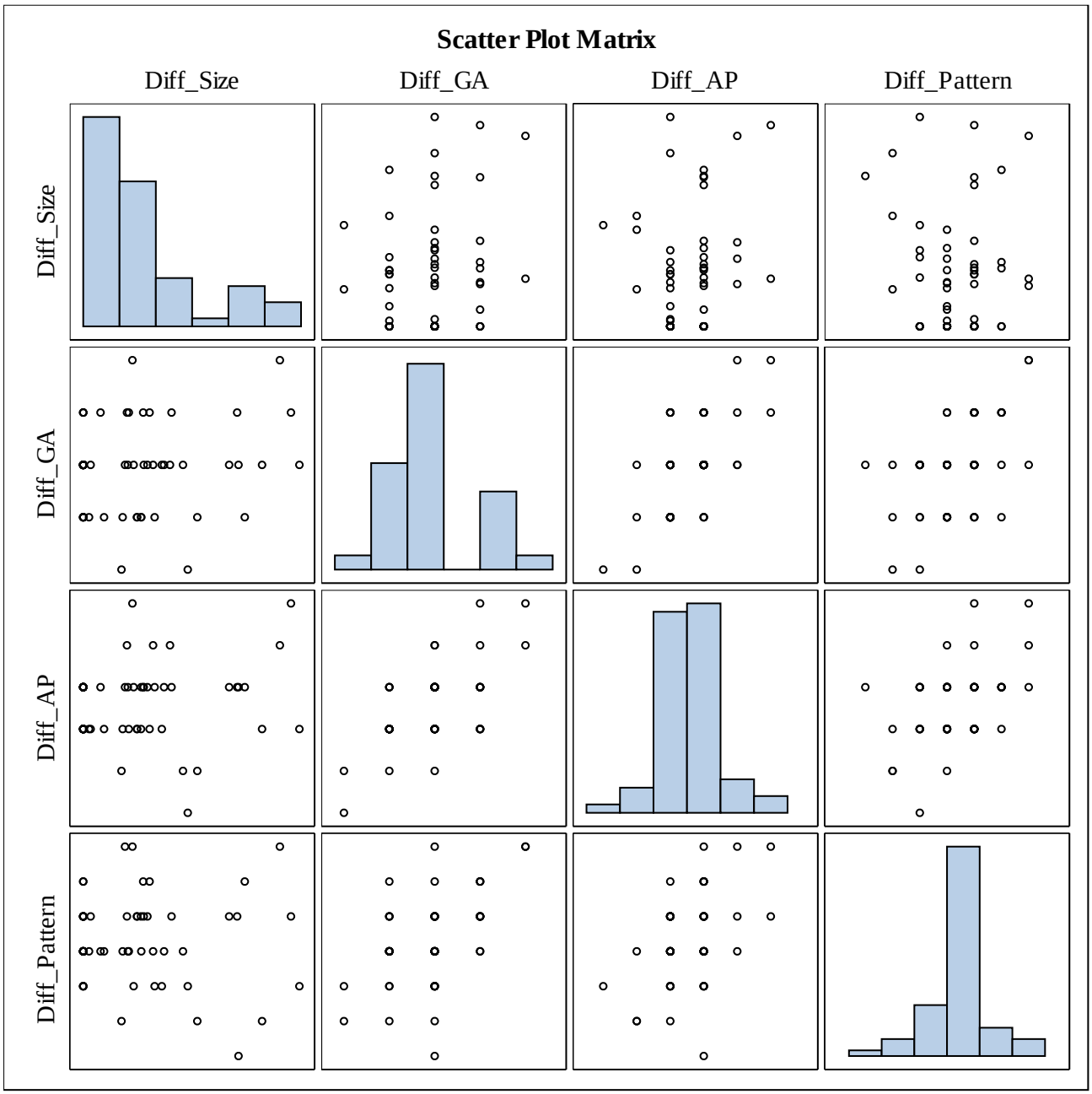


Figure 6: Flash Reflection on the tooth Surface Complicating WSL assessment

TABLES

Table 1: Descriptive Demographic Analysis

	N	**Mean**	**Std Deviation**	**P Value (Sig. < 0.05)**	Post Hoc Intergroup Comparison (Sig. < .05)
AGE at T0				0.02	G1 Vs G2 0.035
G1	24	21.44	11.63		
G2	16	14.83	4.26		G2 Vs G3 0.765
G3	19	14.47	3.99		
Total	59	17.40	8.64		G3 Vs G1 0.012
Time of treatment T2-T0				0.20	
G1	24	16.83	5.11		
G2	16	17.40	6.28		
G3	19	19.52	4.40		
Total	59	17.85	5.29		

Table 2: Summary of the change of WSL Incidence from T0 to T2

Lesion Presence/Absence (Y/N)		Overall (n=59)		Group1(n1=24)		Group2(n2=16)		Group3(n3=19)	
T0	T2	Frequency	Percent	Frequency	Percent	Frequency	Percent	Frequency	Percent
No	No	22	37.29	10	41.67	4	25.00	8	42.11
No	Yes	23	38.98	7	29.17	7	43.75	9	47.37
Yes	Yes	14	23.73	7	29.17	5	31.25	2	10.53

Table 3: Whether the incident change is significantly different among groups

Table of Group by Lesion_T0_T2_change			
Group(Group)	Lesion_T0_T2_change		
Frequency Row Pct	No	Yes	Total
1	10 58.82	7 41.18	17
2	4 36.36	7 63.64	11
3	8 47.06	9 52.94	17
Total	22	23	45

Statistic	Prob
Chi-Square	0.5627

Table 4: Surface Area (SA) change from T0 to T2

Analysis Variable : Diff_SA								
Group	**N**	**Mean**	**Std Dev**	**Median**	**Minimum**	**Maximum**	**Range**	**P Value (Within-group Change) ***
1	**24**	0.066	0.092	0.023	0.000	0.357	0.357	0.0001
2	**16**	0.110	0.095	0.100	0.000	0.296	0.296	0.0005
3	**19**	0.093	0.112	0.081	0.000	0.343	0.343	0.0010

Table 5: Change of Categories from T0 to T2

Lesion Category Change		Overall (n=59)		Group1(n1=24)		Group2(n2=16)		Group3(n3=19)	
T0	**T2**	**Frequency**	**Percent**	**Frequency**	**Percent**	**Frequency**	**Percent**	**Frequency**	**Percent**
0	**0**	22	37.29	10	41.67	4	25.00	8	42.11
0	**1**	21	35.59	6	25.00	7	43.75	8	42.11
0	**2**	2	3.39	1	4.17	0	0	1	5.26
1	**1**	14	23.73	7	29.17	5	31.25	2	10.53

Coding for this table: 0 -None, 1- Mild , 2-Moderate, 3 –Severe. No patient has category 3, neither at T0 nor at T2

Table 6: Correlation of Lesion SA/size change with Periodontal Indices change

Table 6.1

Simple Statistics						
Variable	**N**	**Mean**	**Std Dev**	**Median**	**Minimum**	**Maximum**
Diff_Size	59	0.08652	0.09962	0.07223	0	0.35726
Diff_GA	59	0.93220	0.84821	1.00000	-1.00000	3.00000
Diff_AP	59	0.57627	0.89449	1.00000	-2.00000	3.00000
Diff_Pattern	58	0.31034	1.24544	0	-3.00000	3.00000

GA: Gingival Architecture; AP: Appearance of Plaque; Pattern: Bleeding Pattern

Table 6.2

Spearman Correlation Coefficients Prob > |r| under H0: Rho=0 Number of Observations				
	Diff_Size	**Diff_GA**	**Diff_AP**	**Diff_Pattern**
Diff_Size	1.00000 59	0.08651 0.5147 59	0.16659 0.2073 59	0.00322 0.9809 58
Diff_GA	0.08651 0.5147 59	1.00000 59	0.50263 <.0001 59	0.45426 0.0003 58
Diff_AP	0.16659 0.2073 59	0.50263 <.0001 59	1.00000 59	0.36710 0.0046 58
Diff_Pattern	0.00322 0.9809 58	0.45426 0.0003 58	0.36710 0.0046 58	1.00000 58

Table 7: Reliability for Lesion Presence/Absence (Yes/No) [i.e Size=0 or >0] at T0;

Table 7.1

T0: Within-Rater1 Reliability for Lesion Outcome at T0			
Eval_1st	**Eval_2nd**		
Frequency	**No**	**Yes**	**Total**
No	44	1	45
Yes	1	13	14
Total	45	14	59

Table 7.2

Simple Kappa Coefficient	
Kappa	0.9063
ASE	0.0650
95% Lower Conf Limit	0.7789
95% Upper Conf Limit	1.0000

Table 8: Outcome of Intra-Rater Reliability for Lesion Presence/Absence (Yes/No) [i.e Size=0 or >0] at T0;

Table 8.1

T0: Within-Rater1 Reliability for Lesion Outcome at T2			
Eval_1st	**Eval_2nd**		
Frequency	**No**	**Yes**	**Total**
No	22	0	22
Yes	2	35	37
Total	24	35	59

Table 8.2

Simple Kappa Coefficient	
Kappa	0.9288
ASE	0.0493
95% Lower Conf Limit	0.8321
95% Upper Conf Limit	1.0000

Table 9: Outcome of Intra-Rater Reliability test for measuring the (non-zero) surface area of the lesions

Table 9.1

T0: Within-Rater1 Reliability for Non-zero Size Outcome			
	ICC	Lower bound	Upper bound
T0 (n=28)	0.95200	0.86117	0.98391

n=28 is total number of non-zero size values for T0 images from Rater1 1st reading and 2nd reading.

Table 9.2

T2: Within-Rater1 Reliability for Non-zero Size Outcome			
	ICC	Lower bound	Upper bound
T2 (n=72)	0.97479	0.95144	0.98699

n=72 is total number of non-zero size values for T2 images from Rater1 1st reading and 2nd reading.

Table 10: Outcome of Inter-Rater Reliability for Lesion Presence/Absence (Yes/No) [i.e Size=0 or >0] at T0;

Table 10.1

T0: Between-Rater Reliability for Lesion Outcome			
Rater1	**Rater2**		
Frequency	**No**	**Yes**	**Total**
No	42	3	45
Yes	1	13	14
Total	43	16	59

Table 10.2

Simple Kappa Coefficient	
Kappa	0.8215
ASE	0.0856
95% Lower Conf Limit	0.6538
95% Upper Conf Limit	0.9892

Table 11: Outcome of Inter-Rater Reliability for Lesion Presence/Absence (Yes/No) [i.e Size=0 or >0] at T2;

Table 11.1

T2: Between-Rater Reliability for Lesion Outcome			
Rater1	**Rater2**		
Frequency	**No**	**Yes**	**Total**
No	22	0	22
Yes	1	36	37
Total	23	36	59

Table 11.2

Simple Kappa Coefficient	
Kappa	0.9641
ASE	0.0356
95% Lower Conf Limit	0.8944
95% Upper Conf Limit	1.0000

Table 12: Outcome of Inter-Rater Reliability test for measuring the (non-zero) surface area of the lesions

Table 12.1

T0: Between-Rater Reliability for Non-zero Size Outcome			
	ICC	**Lower bound**	**Upper bound**
T0 (n=30)	0.97397	0.92309	0.99134

n=30 is total number of non-zero size values for T0 images from Rater H.A. 1st reading and Rater A.A. reading.

Table 12.2

T2: Between-Rater Reliability for Non-zero Size Outcome			
	ICC	**Lower bound**	**Upper bound**
T2(n=73)	0.97737	0.95677	0.98822

n=73 is total number of non-zero size values for T2 images from Rater H.A 1st reading and Rater A.A. reading.

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APPENDIX

Interpretation of the kappa coefficients, according to Landis and Koch.

$\kappa \leq 0.2$	Poor agreement
$0.2 < \kappa \leq 0.4$	Fair agreement
$0.4 < \kappa \leq 0.6$	Moderate agreement
$0.6 < \kappa \leq 0.8$	Good agreement
$0.8 < \kappa \leq 1.0$	Excellent agreement

Interpretation of ICC , following guidelines from Cicchetti's paper.

ICC < 0.4	Poor reliability
0.4≤ ICC < 0.6	Fair reliability
0.6≤ ICC <0.75	Good reliability
0.75≤ ICC ≤ 1.0	Excellent reliability